P.J.

E, X and Y may be independently present or absent, and if present are independently selected from the moieties: alkyl, aryl, alkyl-aryl, heteroalkyl, heteroaryl, aryl-heteroaryl, alkyl-heteroaryl, cycloalkyl, alkyl ether, alkyl-aryl ether, aryl ether, alkyl amino, aryl amino, alkyl-aryl amino, alkyl sulfide, alkyl-aryl sulfide, aryl sulfide, alkyl sulfone, alkyl-aryl sulfone, aryl sulfone, alkyl-alkyl sulfoxide, alkylaryl sulfoxide, alkyl amide, alkyl-aryl amide, aryl amide, alkyl sulfonamide, alkyl-aryl sulfonamide, aryl sulfonamide, alkyl urea, alkyl-aryl urea, aryl urea, alkyl carbamate, alkyl-aryl carbamate, aryl carbamate, alkyl -hydrazide, alkyl-aryl hydrazide, alkyl hydroxamide, alkyl-aryl hydroxamide, alkyl sulfonyl, aryl sulfonyl, heteroalkyl sulfonyl, heteroaryl sulfonyl, alkyl carbonyl, aryl carbonyl, heteroalkyl carbonyl, heteroaryl carbonyl, alkoxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, heteroarylaminocarbonyl or a combination thereof, with the proviso that E, X and Y may optionally be additionally substituted with moieties selected from the group consisting of aromatic, alkyl, alkyl-aryl, heteroalkyl, aryl-heteroaryl, alkyl-heteroaryl, cycloalkyl, alkyl ether, alkyl-aryl ether, alkyl sulfide, alkyl-aryl sulfide, alkyl sulfone, alkyl-aryl sulfone, alkyl-aryl amide, alkyl sulfonamide, , alkyl amines, alkyl-aryl amines, alkyl-aryl sulfonamide, alkyl urea, alkyl-aryl urea, alkyl carbamate, alkyl-aryl carbamate, halogen, hydroxylamino, alkyl carbazate, aryl carbazate;

 $R^1 = \mathsf{COR}^5 \text{ or } \mathsf{B}(\mathsf{OR})_2, \text{ wherein } \mathsf{R}^5 = \mathsf{H}, \mathsf{OH}, \mathsf{OR}^8, \mathsf{NR}^9 \mathsf{R}^{10}, \mathsf{CF}_3, \mathsf{C}_2 \mathsf{F}_5, \mathsf{C}_3 \mathsf{F}_7, \mathsf{CF}_2 \mathsf{R}^6, \mathsf{R}^6, \mathsf{COR}^7 \text{ wherein } \mathsf{R}^7 = \mathsf{H}, \mathsf{OH}, \mathsf{OR}^8, \mathsf{CHR}^9 \mathsf{R}^{10}, \mathsf{or } \mathsf{NR}^9 \mathsf{R}^{10}, \mathsf{wherein } \mathsf{R}^6, \mathsf{R}^8, \mathsf{R}^9 \text{ and } \mathsf{R}^{10} \text{ are independently selected from the group consisting of } \mathsf{H}, \mathsf{alkyl}, \mathsf{aryl}, \mathsf{heteroalkyl}, \mathsf{heteroaryl}, \mathsf{cycloalkyl}, \mathsf{cycloalkyl}, \mathsf{arylalkyl}, \mathsf{heteroarylalkyl}, \mathsf{CH}(\mathsf{R}^1)\mathsf{COOR}^{11}, \mathsf{CH}(\mathsf{R}^1)\mathsf{CONR}^{12} \mathsf{R}^{13}, \mathsf{CH}(\mathsf{R}^1)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^3), \mathsf{COOR}^{12} \mathsf{R}^{13}, \mathsf{CH}(\mathsf{R}^1)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{COOR}^{12} \mathsf{R}^{13}, \mathsf{CH}(\mathsf{R}^1)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{COOR}^{12} \mathsf{R}^{13}, \mathsf{CH}(\mathsf{R}^1)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{CONHCH}(\mathsf{R}^3)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{CONHCH}(\mathsf{R}^5)\mathsf{CONR}^{12} \mathsf{R}^{13}, \mathsf{ch}(\mathsf{R}^1)\mathsf{CONHCH}(\mathsf{R}^2)\mathsf{CONHCH}(\mathsf{R}^4)\mathsf{CONHCH}($ 

Z is selected from O, N, or CH;

W may be present or absent, and if W is present, W is selected from C=O, C=S, SO<sub>2</sub> or C=NR;

Q is (NR)<sub>p</sub>, O, S, CH<sub>2</sub>, CHR, CRR' or a double bond towards V;
A is O, CH<sub>2</sub>, (CHR)<sub>p</sub>, (CHR-CHR')<sub>p</sub>, (CRR')<sub>p</sub>, NR, S, SO<sub>2</sub>, C=O or a bond;

G is  $(CH_2)_p$ ,  $(CHR)_p$ ,  $(CRR')_p$ , NR, O, S, SO<sub>2</sub>, S(O)<sub>2</sub>NH, C=O, or a double bond towards E or V;

V is CH, CR or N;

p is a number from 0 to 6; and

R, R', R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of H; C1-C10 alkyl; C2-C10 alkenyl; C3-C8 cycloalkyl; C3-C8 heterocycloalkyl, aryl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro; heteroaryl; alkyl-aryl; alkyl-heteroaryl; (cycloalkyl)alkyl and (heterocycloalkyl)alkyl, wherein said cycloalkyl is made of three to eight carbon atoms, and zero to six oxygen, nitrogen, sulfur, or phosphorus atoms, and said alkyl is of one to six carbon atoms; with said alkyl, heteroalkyl, alkenyl, heteroalkenyl, aryl, heteroaryl, cycloalkyl and heterocycloalkyl moieties may be optionally substituted, with said term "substituted" referring to optional and suitable substitution with one or more moieties selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, heterocyclic, halogen, hydroxy, thio, alkoxy, aryloxy, alkylthio, arylthio, amino, amido,

ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, sulfonamide,

sulfoxide, sulfone, sulfonyl urea, hydrazide, hydroxamate and thiourea,

with the following provisos:

(i) that when

 $R^3 = HOOC-CH_2-CH_2-$ 

Z= N

R⁴= H

W= >C=O

Y= -CH<sub>2</sub>-

X= aryl ether

 $A = -CH_2$ 

E is absent

 $G = -(CH_2)_p$ -, wherein p is 0

Q = -NH-

V= >CH-

and R<sup>2</sup>=-COOH,

then R1 is not a carboxylic acid or carboxylic ester; and

(ii) that when

 $R^3 = H$ 

Z= CH

 $R^4 = H$ 

W, Y, X and E are all absent

A is present or absent

Q= NH

V= CH

R<sup>2</sup>=H

R1= COR5

 $R^5 = N(R^9)R^{10}$ 

 $R^9 = H$ 

R<sup>10</sup>= CH(R<sup>1</sup>)CONHCH(R<sup>2'</sup>)COOR<sup>11</sup>

 $R^{11} = H$ 

R2'= H, and

R1'= alkylheteroaryl,

then G is absent.

Claim 21 (amended): A composition comprising as an active ingredient a compound of claim 1 and a pharmaceutically acceptable carrier.

<u>Claim 22 (amended)</u>: The composition of claim 21 wherein said compound of claim 1 is present in amounts effective to inhibit hepatitis C nonstructural protein-3 protease (HCV NS3 protease).

Please cancel Claim 23 without prejudice.

<u>Claim 26 (amended)</u>: A method of preparing a composition for inhibiting hepatitis C nonstructural protein-3 protease (HCV NS3 protease), said method comprising bringing into intimate contact a compound of claim 1 in an amount effective to cause said inhibition and a pharmaceutically acceptable carrier.

<u>Claim 27 (amended)</u>: A compound exhibiting HCV NS3 protease inhibitory activity, or enantiomers, stereoisomers, rotamers or tautomers of said compound, or pharmaceutically acceptable salts or solvates of said compound, said compound being selected from the group of compounds with structures listed below:

2 anolde

Nort.

D3 Const

H H H OH

HIN HOH

THE HINDS

THE POH

D3/ agrif (D3)

NH<sub>2</sub>
CH<sub>3</sub>

Q3 Conf. HOOC HINT HOOL NH2

60 H

<u>Claim 28 (amended)</u>: A composition for inhibiting hepatitis C nonstructural protein-3 protease (HCV NS3 protease), said composition comprising one or more compounds in claim 27 in amounts therapeutically effective to cause said inhibition and a pharmaceutically acceptable carrier.

<u>Claim 29 (amended)</u>: The composition of claim 28, additionally containing an

Q3 Conclide antiviral agent.

Claim 30 (amended): The composition of

The composition of claim 28 or claim 29, still additionally

containing an interferon.

Claim 31 (amended):

The composition of claim 30, wherein said antiviral agent

is ribavirin and said interferon is  $\alpha$ -interferon.

<u>Claim 32 (new claim)</u>: A method of inhibiting HCV NS3 protease comprising administering a compound of claim 1 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

<u>Claim 33 (new claim)</u>: A method of inhibiting HCV NS3 protease comprising administering a composition of claim 21 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

<u>Claim 34 (new claim)</u>: A method of inhibiting HCV NS3 protease comprising administering a compound of claim 27 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

<u>Claim 35 (new claim)</u>: A method of inhibiting HCV NS3 protease comprising administering a composition of claim 28 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

<u>Claim 36 (new claim)</u>: A method of inhibiting hepatitis C virus replication comprising administering a compound of claim 1 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

<u>Claim 37 (new claim)</u>: A method of inhibiting hepatitis C virus replication comprising administering a composition of claim 21 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

<u>Claim 38 (new claim)</u>: A method of inhibiting hepatitis C virus replication comprising administering a compound of claim 27 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

<u>Claim 39 (new claim)</u>: A method of inhibiting hepatitis C virus replication comprising administering a composition of claim 28 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

## **REMARKS**

Claims 1-31 are pending in the application. Claims 24 and 25 were withdrawn from consideration, thus leaving claims 1-23 and 26-31 under prosecution.

In the instant Office Action, claims 21-23, 26 and 28-31 were rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to